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WARNING LETTER

Food and Drug Administration
Rockville MD 20857

OVERNIGHT DELIVERY

Ref: No. 97-HFD-340-0401

Charles H. Farr, M.D., Ph.D.
Director
International Bio-Oxidative Medicine Foundation, Inc.
5419 South Western Avenue
Oklahoma City, Oklahoma 73189

JUN 2 - 1997

Dear Dr. Farr:

On January 30 and February 5 and 6, 1997, Mr. Lloyd D. Payne, an investigator with the Dallas District of the Food and Drug Administration (FDA), inspected the institutional review board (IRB) at International Bio-Oxidative Medicine Foundation, Inc. (IBOMF). The purpose of this inspection was to determine whether your procedures for the protection of human subjects complied with Title 21 of the Code of Federal Regulations (CFR) Parts 50 and 56 (enclosure #1). These regulations apply to clinical studies of products regulated by FDA.

At the completion of the inspection, Mr. Payne gave a Form FDA 483 (enclosure #2) to Robert L. Santelli, D.C., IRB Chairman, describing the deficiencies identified during this inspection. The deficiencies listed on this Form FDA 483 repeat the deficiencies listed on the Form FDA 483 issued after the previous November 28 and December 5, 12 and 19, 1995 inspection (enclosure #3). Dr. Santelli stated that neither he nor IBOMF had made any attempt to correct the items on the Form FDA 483 from the 1995 inspection.

The Agency has reviewed the documents and records relating to the IRB's responsibilities for the protection of human subjects of research contained in Mr. Payne's inspection report and the objectionable conditions and practices listed in the current Form FDA 483. The evidence shows that the IRB has failed to adhere to pertinent federal regulations as contained in 21 CFR 50 and 56. The Agency's findings represent significant violations of the Federal Food, Drug, and Cosmetic Act.

SUMMARY OF IRB MEMBERSHIP VIOLATIONS [21 CFR 56.107]:

1. The IRB has failed to maintain a membership of at least five members to perform complete and adequate review of research activities.

During the inspection, Dr. Santelli stated to Mr. Payne that the IRB has no members other than himself. Attempts to contact the IRB members since September 1995 have been unsuccessful. This information was also verified by Mrs. Skoshi Farr, Administrative Assistant.

SUMMARY OF IRB FUNCTIONS AND OPERATIONS VIOLATIONS [21 CFR 56.108(a)(4), (b)(1)(2)(3), and (c)]:

2. The IRB's written procedures lacked procedures to ensure that changes in approved research may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects. This is listed on the Form FDA 483 as item 6B.
3. The IRB's written procedures lack procedures to ensure prompt reporting to the IRB, appropriate institutional officials, and the FDA of (1) any unanticipated problems involving risks to human subjects or others; (2) any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB; or (3) any suspension or termination of IRB approval. This is listed on the Form FDA 483 as items 6C, D, and E.
4. The IRB failed to review all proposed research at convened meetings. Two studies were approved by individual votes by telephone. A third study had an approval letter issued by the IRB, but there is no record of a convened meeting at which the study was approved. This is listed on the Form FDA 483 as item 7.

SUMMARY OF CONTINUING REVIEW VIOLATIONS [21 CFR 56.109(a)]:

5. The IRB has failed to conduct continuing review at intervals appropriate to the degree of risk, but not less than once per year. There is no documentation of continuing review of studies at convened meetings in the minutes of the meetings or elsewhere in the IRB's files. This is listed on the Form FDA 483 as item #1.

SUMMARY OF RECORD VIOLATION [21 CFR 56.115(a)(1)(3) and (5)]:

6. The IRB files either lack copies of protocols, investigator brochures, and informed consent documents or contain incomplete study information for studies reviewed and approved by the IRB. This is listed on the Form FDA 483 as items 3, 4, and 8.

7. The IRB lacks documentation that approved research received continuing review at least annually. The one exception was a study which received continuing review at the July 12, 1991 meeting. This is listed on the Form FDA 483 as item 1.
8. The IRB's membership rosters lack sufficient information to describe each member's chief anticipated contributions to IRB deliberations or to determine the relationship between each member and the institution. This is listed on the Form FDA 483 as item #9.

SUMMARY OF INFORMED CONSENT VIOLATIONS (21 CFR 31.25(a)(1)(2) and (4)):

9. The informed consent for the [REDACTED] study lacked a statement that the study involves research and a description of any reasonably foreseeable risks or discomforts. This is listed on the Form FDA 483 as item 5A.
10. The informed consent documents for the following studies lack disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject:
 - a) [REDACTED]
 - b) [REDACTED]
 - c) [REDACTED]

This is listed on the Form FDA 483 as items 5 A, B, and C.

The above cited violations may not be all inclusive of the deficiencies in your IRB operation.

We note that in the middle of the current inspection, new IRB members were recruited and a meeting was held on February 4, 1997. Dr. Santelli announced at the meeting that all studies, with exception of the [REDACTED] were terminated due to lack of progress reports. Progress reports for the [REDACTED] submitted by [REDACTED]

It is not documented in the February 4, 1997 minutes of meeting that any information (including the names of the studies and the clinical investigators) for previously approved studies was supplied to the IRB members for review or that

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the IRB members were informed of the letters issued to clinical investigators on January 31, 1997 (discussed below). The next IRB meeting is scheduled for October 1, 1997.

Your January 31, 1997 letters to clinical investigators request information on any active studies that the investigators may be participating in and state that the "I.R.B. will be closing all investigation studies by March 1, 1997 unless the I.R.B. committee receives in writing information that would suggest you would like to continue with your study."

We believe that the February 4, 1997 IRB meeting was ineffective to ensure that the rights and welfare of research subjects are being adequately protected. As indicated by the January 31, 1997 letters, the IRB does not have accurate records of currently active studies and can not, therefore, perform continuing review or terminate any studies. The scheduling of the next IRB meeting for October 1, 1997 indicates that the IRB does not plan to hold a timely convened meeting to review information received as a result of the January 31, 1997 letters.

We have no assurance that your IRB activities and responsibilities for insuring that the care of research subjects are in compliance with FDA regulations. We are concerned that your lack of written procedures will not adequately protect the rights and welfare of human subjects of research. Therefore, in accordance with 21 CFR 56.120(a)(1) and (2), we are invoking the following sanctions against your IRB:

- a) You are to withhold approval of all new studies, subject to the requirements of 21 CFR Parts 50 and 56, that are conducted at your IRB's institution, or other clinical studies that are under review and pending approval by IBOMF: and
- b) You are further directed not to allow any new subjects to enter in or be added to opened studies that are subject to 21 CFR Parts 50 and 56.

If procedures have been implemented, we request that you submit a copy of these written procedures to us as part of your response to this letter. If appropriate written procedures have not yet been put in place, or are not put into place immediately, we may take further administrative sanctions as authorized by 21 CFR 56.120 and 56.121. These sanctions may include, but are not limited to, the termination of all previous studies approved by your IRB and disqualification of your IRB.

Please inform this office, in writing, within fifteen (15) working days from the date of receipt of this letter, of the corrective actions you have taken or plan to take to bring your IRB into compliance with FDA's regulations. You should also include the following:

- a) any actions taken to turn over responsibility of any future IRB review to another IRB until such a time as the IBOMF IRB has demonstrated that the IBOMF IRB can meet the requirements of 21 CFR 50 and 56;
- b) a list of all studies and clinical investigators, including the number of subjects active at each site; and,
- c) copies of any letters or other documentation of actions taken.

If you have any questions, please contact Mr. Anthony E. Rodgers at (301) 594-1026 or Fax (301) 594-1204. Your response should be addressed to the following:

Anthony E. Rodgers, Acting Team Leader
Human Subject Protection Team, HFD-343
Division of Scientific Investigations
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, Maryland 20855

Sincerely yours,



David A. Lepay, M.D., Ph.D.
Director
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research

Enclosure #1 FDA Regulations Parts 50 and 56
Enclosure #2 Form FDA 483 (January and February 1997 inspection)
Enclosure #3 Form FDA 483 (November and December 1995 inspection)

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cc:

Robert L. Santelli, D.C.

Chairman

Institutional Review Board

International Bio-Oxidative Medicine Foundation, Inc.

5419 South Western Avenue

Oklahoma City, Oklahoma 73189